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(54) Improved infant formula, protein hydrolysate for use in such an infant formula, and method for producing such a hydrolysate

(57) The invention relates to an infant formula, comprising

a) at least one protein component; and
b) at least one lipid component that can be easily digested by an infant;

and optionally one or two of:

c) at least one prebiotic component;
d) at least one viscosity improving component;

and optionally one or more components of infant formula known per se,

characterised in that: the protein component a) has a phosphorous content of less than 0.75 g P/100 g protein.

The formula is preferably further characterised in that the at least one lipid component b) comprises at least one fatty acid triglyceride and/or a mixture of fatty acid triglycerides, in which:

- palmitic acid residues make up more than 10 % all fatty acid residues present in the triglycerides; and in which:

the triglycerides in which the palmitate residue is in the Sn1- or Sn3-position make up no more than 16 % of all triglycerides present.

The invention also relates to a method for preparing a protein hydrolysate, in particular for use in the formula of the invention.

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Description

[0001] The present invention relates to an improved infant formula.

[0002] In infants, in particularly in infants of less than 6 months months old, the digestive system has to develop and adapt to food. Because of this, for the first months of their lives, infants are usually fed specialized infant formulas.

[0003] Usually, such infant formulas are well tolerated. However, in a limited number of cases, conventional formulas may lead to minor problems, in a particular with respect to the processes that occur in the gastrointestinal tract.

[0004] More in particular, in the research leading up to the present invention, it was acknowleged by the inventors that conventiontal formulas may lead to undesired disturbances in the natural gutflora and/or to an unnatural gutflora. Also, it was acknowleged that conventional infant formulas may provide the wrong type and/or the wrong amounts of substrate; and/or may have the wrong composition of diet components.

[0005] Such defects in conventional formulas may lead to undesired processes in the gastointestinal tract and/or to an undesired disturbance of the natural processes. In turn, this may lead to symptoms such as:

- an undesirable constitution of faeces (e.g. diahrrea, constipation or unnatural colorur tone);
- high local gas production, which may result in cramps in the infant gut and/or to bloating and delayed stomach emptying;
- a decreased bioavailability of divalent cations;
- undesired levels of agressive agents in the faeces, in particular agents that can irritate and/or damage the epithelial cells (such as those of the lining of the gastrointestinal tract and/or the skin) including but not limited to proteases.

[0006] As a result, infants which are fed conventional formulas may suffer from reduced appetite and/or regurgitation of food (often in case of disturbances in the gut). Also, disturbances in the natural proces of stomach emptying and an irregular consumption pattern may occur, which may cause hunger, as a result of which infants may consume large volumes of formula too hastily, which in turn may lead to excessive acrophagia and/or regurgitation.

[0007] Also, as a result of the problems, causes and/or factors indicated above, infants which are fed conventional formulas may suffer from an imparted immune function which may become evident in rapid development of a rash on the skin of the bottom; undernourishment (imparted growth), malfunctioning (colic) and even damage to the gut (intolerances to food components).

[0008] Thus, there is a need for an infant formula that has improved characteristics with respect to the prevention and/or alleviation of one or more, and preferably all, of the abovementioned problems. The present invention provides such an infant formula.

[0009] In this respect, it is of importance that the formula of the invention is capable of preventing, alleviating and/or reducing all of the abovementioned problems simultaneously. This is because, in particular for a parent, it may be difficult to establish the specific cause of the problem(s). Thus, by using an infant formula of the invention that can prevent and/or alleviates all of these problems simultaneously, parents may be assured that by the use of the infant formula of the invention, all such problems can be reduced, irrespective of the cause thereof, and without having to switch from one formula to another until one has found an infant formula that reduces the presently occurring problem (s) without causing any of the other problem(s) mentioned above.

[0010] Usually, when one or more of the above problems occur/persist, a parent will usually switch to another formula or - if that does not help - consult a pediatrician. However, of all infant formulas currently on the market, none has characteristics that can prevent or alleviate all of the abovementioned problems simultaneously. Thus, the switching to another formula may not reduce the problem and/or may lead to one or more of the other problems mentioned above. Also, the infant may have problems getting used to (the taste of) the new formula, which may lead to a reduction in appetite. The latter may in particular be a problem when - because of the abovementioned problems - the formula is or has to be changed several times.

[0011] In the research leading up to the present invention, it was acknowleged by the inventors that some of the major causes of the disturbance(s) of the processes in the gastrointestinal tract as may occur with conventional infant formulas include:

- the fact that, in the triglycerides present in the (lipid component of) conventional infant formulas, undesirably high amounts of palmitic acid, myristic acid, and/or stearic acid are present in the Sn1 - or Sn3-position of glycerol;
- the fact that conventional infant formulas contain undesirably high amounts of divalent cations, and in particular undesirably high amounts of calcium ions. In particular, this is a problem when at the same time, there are high amounts of palmitic acid, myristic acid, and/or stearic acid are present in the Sn1 - or Sn3- position of the triglycerides present, i.e. as mentioned above;
- the fact that conventional infant formulas contain insufficient amounts of suitable substrates for micro-organisms, i.e. for the naturally occuring intestinal flora.

[0012] Thus, according to the invention, these abovementioned problems are solved by the following measures, which result in an infant formula according to the claims.

[0013] Firstly, an infant formula is provided that - in the lipid/triglyceride components present therein - does not contain high amounts of these saturated fatty acids in the Sn1- or Sn3- position of glycerol, and in particular does not contain high amounts of palmitic acid in the Sn1- or Sn3- position. This can be achieved by using, in the preparation of an infant formula of the invention, a lipid component that:

- contains lipids that have relatively large amounts of C14:0, C16:0 and C18:0 in the Sn2 position of glycerol, such as specific phospholipids or triglycerides of animal, microbial or plant origin, in which the triglycerides have been subjected to enzymatic or other re-esterification such that the palmitic acid residues are for a large part present in the 2-position;
- contains a relatively small amount of fatty acids of the type C14:0, C16:0 and C18:0, especially C16:0.

[0014] Secondly, an infant formula is provided that contains a relatively low amount of divalent cations, especially of magnesium and/or calcium, and in particular a low amount of calcium ions, e.g. in the amounts mentioned below.

[0015] In conjunction within addition to (or even instead of) these low amounts of calcium, according to the invention the bio-availability of said cations may be improved; for instance by assuring that, at pH 6-7 (e.g. under the conditions prevalent in the duodenum), most of the calcium salts provided by the formula of the invention are in the form of water soluble salts (e.g. no or only low amounts of basic phosphate and/or citrate salts).

[0016] Also, as mentioned below, preferably the amount of phosphorous in the infant formula should be as low as possible, e.g. as defined below. Inter alia, according to the invention, this is achieved by using proteins, and in particular protein hydrolysates, with a low phosphorous content, as further described below.

[0017] In this respect, the use of a protein hydrolysate also ensures that the protein components present in the infant formula of the invention do not sensitize the infants. The use of the hydrolysates also ensures that the protein components can be easily absorbed from the gastrointestinal tract, and thus do not interfere (too much) with the processes occuring in the intestines (and in particular in the colon).

[0018] Also, as will be further described below, the use of a protein hydrolysate - in conjunction with the favorable osmotic value provided by the formula of the invention - will promote the natural processes of stomach emptying, which will prevent and/or reduce regurgitation.

[0019] Thirdly, an infant formula is provided that contains a sufficient amount of substrate for creation and maintenance of a beneficial flora in the whole gut, especially in the colon. This ensures a uniform production of gas and beneficial substances such as short chain fatty acids, and also prevents the release of excessive amounts of agressive agents. In human breast milk lactose and oligosaccharides provide this substrate. In conventional infant fomula lactose is the only source. It has been found that, most preferably, a source of oligosaccharides is present in the general purpose formula according to the invention, e.g. in addition to and/or instead of lactose, the latter especially for those infants that are intolerant to lactose.

[0020] Thus, the present invention provides an infant formula that comprises any combination of two or more, preferably of three or more, and most preferably all, of the following components:

a) at least one protein component (hereinbelow also referred to as "*component A*");
b) at least one lipid component that can be easily digested by an infant ("*component B*");
c) at least one prebiotic component ("*component C*)";

at least one viscosity improving component ("*component D*");
and that optionally further contains any component of infant formula known per se, including but not limited to those described hereinbelow (hereinbelow referred to as *"further components"*); and in which the components A to D and the one or more further components are preferably as described hereinbelow.

[0021] The protein component may comprise whole proteins and/or a protein hydrolysate, or a mixture thereof, and is most preferably low in phosphorous, e.g. a phosphorous content of less than 0.75 g/100g protein. Also, when whole proteins are present, they are most preferably such that they are easily digested by the infant, e.g. as described below.

[0022] Preferably, the entire infant formula of the invention has a phosphorous content as defined on pages and 9 below

As the source of the protein component preferably mammalian milk, e.g. bovine milk, goats milk or horses milk, is used

[0023] In particular, an infant formula of the invention may be characterised in that:
the protein component a) is a protein hydrolysate, obtained by hydrolysing a starting material comprising a milk protein, a mixture of milk proteins, and/or a milk protein preparation with a combination of at least one endo- and at least one exoproteinase;
and may further be characterised in that:

the at least one lipid component b) comprises at least one fatty acid triglyceride and/or a mixture of fatty acid triglycerides, in which:

- palmitic acid residues make up more than 10 %, preferably 16 - 24 %, of all fatty acid residues present in the triglycerides; and in which,
- triglycerides in which the palmitate residue is in the Sn1 - or Sn3-position make up no more than 16 %, more preferably no more than 13, and most preferably no more than 10.7 %, of all triglycerides present.

[0024] Most preferably, an infant formula of the invention - e.g. containing any two or more, and preferably three or more of the components A to D as mentioned above - is further characterised in that said formula for the most part, and preferably essentially only, contains calcium ions that have a high biological availability, e.g. as described below.

[0025] Preferably, the infant formula of the invention is the form of powder, that prior to use is dissolved by the end-user (i.e. the parent) in warm or cold, and preferably luke-warm, water or another suitable liquid carrier, e.g. in an amount of 9 - 17 g powder per 100 ml water. Both said powder, optionally packaged in a suitable container such as a tin, a box, a bag, a flask or a sachet, as well as the ready-to-use formula obtained by dissolving the powder, form aspects of the invention.

[0026] Preferably, the infant formula of the invention contains at least one component A and/or at least one component B in the amount(s) indicated hereinbelow, i.e. in combination with at least one, preferably at least two, and most preferably all three of the other components [B to D] or [A, C and/or D], respectively; and optionally one or more further components.

[0027] More preferably, the infant formula of the invention contains a combination of components A + B + C; and optionally one or more further components.

[0028] Generally, in a preferred formula containing at least components A and B, the relative amounts of the above components will be generally as follows:

- Component A: 6.4 to 16.0 wt.%
- Component B: 18 to 29 wt.%
- Component C: 0 to 15 wt.%
- Component D: 0 to 15 wt.%
- Further components: 0 to 60 wt.%

to a total of 100 wt.% of the final formula (e.g. of the powdered formula).

[0029] In a more preferred infant formula containing at least components A, B and C, the relative amounts of the above components will generally be as follows:,

- Component A: 6.4 to 16.0 wt.%
- Component B: 18 to 29 wt.%
- Component C: 3,0 to 15 wt.%
- Component D: 0 to 15 wt.%
- Further components: 0 to 60 wt.%

to a total of 100 wt.% of the final formula.

[0030] In the infant formula containing all four components A, B, C and D, the relative amounts of the above components will generally be as follows:,

- Component A: 6.4 to 16.0 wt.%
- Component B: 18 to 29 wt.%
- Component C: 3.0 to 15 wt.%
- Component D: 1.5 to 15 wt.%
- Further components: 0 to 60 wt.%

to a total of 100 wt.% of the final formula.

[0031] It is envisaged that several infant formulas of the invention may be developed, e.g. with different properties, a range of tastes, and/or for different ages of the infant.

[0032] It is further envisaged that such formulas may differ as to which of the components A to D and further components are present; which particular compunds/ingredients are used as components A to D and/or as further components; and/or in the (relative) amounts of thereof.

[0033] In particular, it is envisaged that there may be developed infant formulas of the invention intended for infants

less than 6 months old, as well as infant formulas of the invention intended for infants of more than 4 months old, and in particular more than 6 months old. These will be further discussed below.

[0034] The proteins that are preferably used as component A have a relatively low phosphorous content. 100 g protein must provide less than 0.75 g phosphorous, preferably less than 0.72 g and even more preferably less than 0.69 g. Whey proteins, dephosphorylated casein or soy protein and mixtures thereof, as well as specific protein fractions from caseins - such as those from which part of, and preferably most, α-caseins have been removed - are suitable sources

[0035] The protein hydrolysates that are preferably used as component A form a further and separate aspect of the invention, as does the method for preparing said preferred hydrolysates. It is envisaged that these hydrolysates may find other applications besides their use in the formulas of the invention, as further discussed below.

[0036] The preferred protein hydrolysates A - when used in the amounts indicated hereinbelow - will generally provide the final formula of the invention with one or more - and preferably all - of the following properties:

- a peptide profile - i.e. for the proteins derived from the hydrolysate - as described hereinbelow;
- a good taste, and in particular a taste that is not bitter, which is an extremely important characteristic for infant formulas in general, and for the infant formulas of the invention in particular;
- a content of free amino acids of less than 10 g, and preferably less than 7 g per 100 g protein equivalent (calculated by multiplying the Kjeldahl nitrogen by 6.25; in which the amount of nitrogen that is measured is determined by the amount of proteins, peptides, amino acids and other nitrogen sources in the product), based upon the final formula;
- an osmolality of less than 270 mOsmol/l, preferably less than 240 mOsmol/l, most preferably less than 230 mOsmol/l. Inter alia, an osmotic value in this range will assure that the infant formual of the invention will not disturb (e.g. inhibit) the natural process of stomach emptying in the infant;
- low sensibilisation, for instance as determined by the tests described by J.J. Pahud and K. Swartz in *Proc of the Tropical Conference, Virginia 1985,* AOAC, 264-271; and/or Piacentini at al., *Allergy* 1994, 48, 361-364 or any other suitable test.

In the tests described by Pahud and Swartz or by Piacentini, the infant formula of the invention preferably shows a degree of sensitisation properties that is preferably essentially zero.

[0037] Furthermore, according to one preferred aspect, when the infant formula of the invention contains the preferred lipid component B described hereinbelow, the formula of the invention may have a reduced overall fat content, compared to conventional infant formulas. According to this aspect of the invention, the infant formula of the invention may have an overall fat content (expressed as total lipid content) of less than 46 wt.%; as compared to 48 wt.% or more for conventional infant formulas.

[0038] In the formula of the invention, Medium Chain Triglycerides (MCTs) can be used to replace partially triglycerides containing palmitic acid residues. If so, it is preferred that such MCTs are used in an amount of less than 20 wt.% of the total lipid component B.

[0039] Also, as further discussed below, when the infant formula of the invention contains the preferred lipid component B, an infant formula of the invention may not require amounts of calcium to be present, that are as high as the calcium contents required in conventional formulas.

[0040] In particular, according to this aspect of the invention, an infant formula of the invention for infants of less than 6 months old may have a calcium content (expressed as mg of calcium per 100 kcal of energy content of the formula) of less than 80 mg/100kcal, and preferably less than 77 mg/100 kcal (e.g. 70 mg/100kcal); as compared to 82-120 mg/100 kcal for conventional infant formulas. In order to provide sufficient calcium to the infant, the concentration of calcium should be above 50 mg/100kcal.

[0041] An infant formula of the invention for infants of more than 6 months old may have a calcium content (expressed as mg of calcium per 100 kcal of energy content of the formula) of less than 122 mg/100kcal, and preferably less than 116 mg/100 kcal (for example 110 mg/100kcal); as compared to 125 mg /100kcal or more for conventional infant formulas.

[0042] Such a reduced calcium content may have certain advantages, such as decreased formation of fatty acid soaps in the gut and more natural exposure of calcium ions to the enterocytes in the duodenum and other parts of the gut and to the gutflora. In addition it was found that less technological problems related to sedmentation occured, e.g. during the preparation of the formula.

[0043] Calcium is preferably added to the infant formula of the invention as soluble salt(s), such as the hydroxide or chloride salts. Tribasic phosphate and citrate salts are insoluble. In addition, it is aimed to prevent that during manufacture insoluble calcium salts are formed, such as phosphates and/or citrates.

[0044] Also, as in infant formula the amount of phosporous present is generally dependant upon the calcium content, in that in conventional infant formula the ratio of calcium-to-phosphorous is generally between 1.5 and 2.0, and usually

about 2, the infant formula of the invention may also have a reduced phosphorous content.

[0045] For instance, based upon the calcium contents mentioned above and a general calcium-to-phosphorous ratio about 2, an infant formula of the invention for infants of less than 6 months old may have a phosphorous content (expressed as mg of phosphorous per 100 kcal of energy content of the formula) of less than 40 mg/100kcal, and preferably less than 38,5 mg/100 kcal (e.g. 38 mg/100kcal); whereas an infant formula of the invention for infants of more than 6 months old may have a phosphorous content (expressed as mg of phosphorous per 100 kcal of energy content of the formula) of less than 61 mg/100kcal, and preferably less than 58 mg/100 kcal (e.g. 38 mg/100kcal).

[0046] Such a reduced phosphorous content may have certain advantages, such as less sedimentation during manufacture and increased bioavailability of divalent cations.

[0047] When besides the phosphorous provided by proteins and/or phospholipids extra phosphorous has to be added, this is especially done by adding monobasic phosphates, preferably from sodium and/or potassium.

[0048] Alternatively, when an infant formula of the invention has a reduced calcium content as described above, the formula of the invention may be prepared a reduced calcium-to-phosphorous ratio of between 1.4 and 2. Such a reduced calcium-to-phosphorous ratio may also have certain advantages, such as to compensate for certain properties of the water that is used by the final user to prepare the formula, e.g. by dissolving the powdered formula of the invention.

[0049] Also, when one or more prebiotic components C are present in the infant formula of the invention, the content thereof is preferably at least 0.3 g/100 ml of the total formula, more preferably at least 0.6 g/100 ml of the total formula. When the formula is given to infants in the usual amounts - e.g. of at least about 200 ml per day (mainly depending upon the age of the infant) as one or more, and preferably 4 or more , feedings per day - this will correspond to a total daily dose of prebiotic components of at least 1.8 g/day (again mainly depending upon the age of the infant).

[0050] Furthermore, when one or more viscosity improving components D are present, the viscosity of the final formula is preferably between 20 and 100 cps, more preferably between 40 and 80 cps; as measured in a Brookfield viscosimeter at 30 rpm.

[0051] Also, the infant formula of the invention preferably has a pH in the range of 4.0 to 7.5.

[0052] Furthermore, according to one specific embodiment of the invention, the infant formula of the invention may (also) have a low lactose content, in order to prevent and/or reduce the problems associated with lactose intolerance and/or reduced lactase activity in the colon. In this embodiment, the infant formula of the invention contains any combination of at least two, preferably at least three, and most preferably all four components A to D; and has a lactose content of at most 6,0 g/100 ml, preferably less than 4,5 g/100 ml, more preferably less than 3,0 g/100 ml of the total formula, as determined by an assay for lactose content known per se.

[0053] Such a formula may be of importance for infants that are lactose intolerant and/or that are suspected to be lactose intolerant, e.g. because they are premature and/or because they (may) have a low lactase activity, e.g. due to hereditary factors.

[0054] The infant formula of the invention may generally be prepared by mixing/combining the different components/ingredients in the amounts mentioned herein. This may generally be carried out in a manner known per se using well known mixing and/or processing equipment. The infant formula may also be heated/sterilized (e.g. by UHT-treatment) and is then preferably brought into a powder form, e.g. by evaporation or (spray-)drying; and aseptically packaged, e. g. in a suitable container such as a tin, a box, a bag, a flask or a sachet. A preferred method for preparing the infant formula of the invention, starting from the preferred hydrolysates used in the invention, will be discussed in more detail hereinbelow.

[0055] The components A to D and any further components to be used in the invention will now be further discussed hereinbelow. In this respect, it will be clear to the skilled person that any component or ingredient used in the infant formula of the invention should be acceptable for use in food products, and in particular be acceptable for use in infant formulas. Also, any component(s) or ingredients used should preferably be compatible with the other components/ingredients of the final formula, and more preferably should also not detract (too much) from the desired properties of the final formula, including but not limited to those provided by any of the other components/ingredients.

I: Component A:

[0056] Component A comprises intact proteins, a protein hydrolysate, or a combination thereof.

[0057] Component A is preferably such that it has a low phosphorous content and is preferably also such that it is easily digestible. Also, preferably, this protein source provides all amino acids that are required for optimal growth, and in sufficient amounts. Suitable sources include specific fragments of proteins from mammal milk or dephosphorylated protein from plant origin such as soy. Most preferably, for infants that could be intolerant to intact proteins, the proteins must be hydrolysed.

[0058] Preferably, this is a hydrolysate obtained by the hydrolysis of one or more milk proteins, in particular from cow's milk, including but not limited to proteins, protein fractions and/or protein preparations derived from whole milk, skimmed milk, casein and/or whey.

[0059] In principle, any milk protein hydrolysate known per se that is suitable for use in food products, more in particular that is suitable for use in infant formula, may be used; and such protein hydrolysates are well known in the art.

[0060] Preferably, the protein hydrolysate used has one or more, and preferably all, of the characteristics a) to e) described hereinbelow. In this respect, although it is not excluded that some prior art methods may afford a protein hydrolysate that has one or more of the desired characteristics a) to e) - and such hydrolysates may be used in the infant formula of the invention - the present invention also provides a range of preferred protein hydrolysates, as well as a method for preparing such hydrolysates, which simultaneously show all desired characteristics a) - e). The use of these hydrolysates is particularly preferred.

[0061] In particular, a protein hydrolysate used in the invention should have one or more and the following characteristics:

a) the hydrolysate should contain all amino acids necessary for good growth of the infant;

b) at least 50% by weight of the peptides present in the hydrolysate (based upon all protein components present in the mixture, including any free amino acids) should have a chain length of between 2 and 30 amino acids, preferably of between 2 and 15 amino acids, and more preferably of between 3 and 12 amino acids; the remainder being either protein components with more amino acids in the protein chain, and/or free amino acids. Preferably, of these remaining protein components, between 0.5 to 8%, more preferably between 0.7 to 7%, and even more preferably between 0.5 and 5%, will have a chain length of more than 30 amino acids.

The presence of small oligopeptides improves the digestability of the proteins, and thereby of the entire formula. Also, the presence of oligopeptides of between 15 and 30 amino acids will allow the digestive system of the infant to get used to larger and/or intact peptides;

c) a low osmolality, due to a low content of free amino acids and salts. This prevents disturbances of the gastrointestinal tract/digestive system such as diarrhea, or at least (further) reduces the risk thereof and prevents a low rate of emptying of the stomach. In this respect, it should be noted that, as the infant formula of the invention is in particular intended for infants that have problems adapting to food/infant formula - e.g. that suffer from one or more of the problems mentioned above - it is important that the present formulas may have a high protein content, if desired. This makes controlling the osmolality of the hydrolysate used in preparing the infant formula of the invention all the more important.

Also, as mentioned below above, a low content of free amino acids is of importance as such free amino acids may provide the hydrolysate - and thereby the entire formula - with a bitter taste. For masking this bitter taste, sweeteners would need to be added to the formula, in particular sweeteners containing many free sugars such as a glucose syrup or certain hydrolysates of starch (e.g. of maize or pea) These, however, generally have a high osmolality (such as those starch hydrolysates having a DE value of > 35), which in turn would increase (too much) the osmolality of the final formula.

Thus, it is another object of the invention to provide a protein hydrolysate-based infant formula that can contain less sweeteners and/or sweeteners with a low osmolality (e.g. with a DE value of less than 30).

Preferably, as mentioned above, the osmolality of the hydrolysate is such that - when the hydrolysate is incorporated in the infant formula in the amounts indicated herein - the osmolality of the final formula is less than 270 mOsmol/l, preferably less than 240 mOsmol/l, most preferably less than 230 mOsmol/l;

d) a good taste, and in particular a taste that is not bitter, which is an extremely important characteristic for (protein hydrolysates for use in) infant formulas.

The taste, and in particular the bitterness, of a protein hydrolysate may for instance be determined in a comparative test involving a taste panel and the use of a suitable compound such as caffeine or a standard hydrolysate as a reference.

In particular, in the taste panel test described in Example 2 of US-A-5,837,312 using a 5% solution of the compound to be tested and using caffeine as the reference, any hydrolysate to be used in the infant formula of the invention should preferably have a bitter taste of less than 2.7; preferably less than 2.4, most preferably between 1.6 and 2.3 (on a scale from 1 to 6 with 6 being the value for the reference caffeine).

As is known in the art, the bitter taste of protein hydrolysates is (at least in part) due to the presence of free amino acids that are formed during hydrolysis, such as free phenylalanine and/or tyrosine). Thus, in the hydrolysates to be used in the invention, the amount of such free amino acids should be as low as possible, i.e. no more than 10 wt.%, and preferably no more than 7 wt.% of all protein components (including the free amino acids).

e) a rate of low sensibilisation, for instance as determined by the tests described by J.J. Pahud and K. Swartz in *Proc. of the Tropical Conference, Virginia 1985,* AOAC, 264-271; and/or Piacentini at al., *Allergy* 1994, 48, 361-364 or any other suitable test. In particular, the hydrolysate is such that - when the hydrolysate is incorporated in the infant formula in the amounts indicated herein - the final infant formula of the invention preferably shows a degree of sensibilisation in the tests described by Pahud and Swartz or by Piacentini, of essentially zero less than [*eventueel aanvullen*].

As is known in the art, the allergenic properties of a hydrolysate - and thereby of the infant formula in which it is incorporated - is for a large part dependant upon the kinds and amounts of peptides that are formed during/that remain after hydrolysis. In this respect, the use of a protein hydrolysate prepared as described below is particularly advantageous.

Although imbalances in the osmolality of the protein hydrolysate can be corrected by removal of ions via techniques that are known in the art, it is highly desirable that hydrolysates fulfill all characteristics a) to e) mentioned above. Such a hydrolysate can be prepared in a reliable manner via the method described below.

[0062] Preferably, the hydrolysate is present in the infant formula of the invention in an amount between 1 and 3 g/ 100 ml, more preferably between 1.3 and 2.0 g/100 ml, and most preferably between 1.6 and 1.9 g/ 100 ml of the total formula.

II: Method for preparing the preferred protein hydrolysates suitable for use as component A in the invention, and use of said hydrolysate in preparing the infant formula of the invention:

[0063] As mentioned above, this method as well as the hydrolysates obtained by it form separate aspects of the invention.

[0064] As the starting material for the hydrolysis of the invention, any protein, mixture of proteins or protein preparation that has a phosphorous content of less than 0.75 g/1 10 g protein can be used . The use of proteins from mammal milk , in particular bovine milk such as whey, in particular acid whey; dephosphorylized casein; β-casein or a suitable mixture thereof is particularly preferred.

[0065] Most preferably, the protein starting material has a phosphorous content of < 0.72 g P/100g protein, most preferably < 0.69 g P/100g protein. Again, these will include whey, in particular acid whey; dephosphorylised casein; or specific casein fractions with reduced α-casein content and/or increased β-casein content.

[0066] Optionally, the starting material may be treated to remove any (remaining) native enzymatic activity.

[0067] Also, optionally, a suspension of yeast cells, optionally homogenized and heated and/or pre-treated to crush the cell walls, may be added to the starting material prior to use in the hydrolysis of the invention, e.g. in an amount of 1-8 g dry mass of yeast cells per 100 g protein. For instance, a mixture of acid whey containing 4 % yeast protein (for instance added as a suspension of 10% Baker's yeast) may be used.

[0068] The starting material - as such or in a suitable form such as a solution or suspension - is then treated with a combination of at least one endo- and at least one exoproteinase, in which said enzyme mixture is added in an amount of 0,1-5 %, based on the starting material.

[0069] The one or more endo- and exoproteinases can be used sequentially - e.g. in two or more separate hydrolysis steps - or simultaneously, e.g. as a suitable mixture in a single hydrolysis step, optionally in combination with one or more further hydrolysis steps using any remaining enzymes.

[0070] Preferably, the hydrolysis comprises a single hydrolysis step using a combination of all enzymes to be used.

[0071] Preferably, as the endo- and exoproteinases, a suitable mixture of serine proteases is used, including but not limited to a suitable enzyme mixture containing (at least) the enzymes Alcalase® and Trypsine® (both available from Novo Nordisk). Another enzyme suitable for use in said enzyme mixture is Flavourzyme® (also available from Novo Nordisk).

[0072] Particularly preferred is the use of a mixture of Alcalase, Flavourzyme and Trypsine in a relative amounts of about 5-10 parts Alcalase to 3-5 parts Flavourzyme to 1 part Trypsine (such as for instance a 7,5 : 4 : 1 mixture) which mixture is most preferably used in an amount corresponding to at least 0.1% - e.g. about 0.2% - Trypsine per 100 g of starting protein.

[0073] By using such a preferred mixture in the manner described below, a hydrolysate can be obtained that, despite the presence of relatively high molecular weight peptides/proteins , is non-sensibilizing. Applying the conditions as described above allows the preparation of an infant formula of a not-bitter taste and a low osmolality (e.g. as described above).

[0074] Using a mixture of endo- and exoproteinases - and in particular of the preferred mixture of Alcalase, Flavourzyme and Trypsine - the starting material is hydrolysed at a temperature of about 45-60 °C, preferably between 50 and 58 °C, for less than 4 hours, preferably from 1.5 to 3 hours .

[0075] During the hydrolysis, the pH is kept in the range of 6.4 to 8, and preferably kept essentially constant, e.g. in the range of 6.8 to 7.8.

[0076] Generally, the degree of hydrolysis is not critical. In other words, independant upon the final degree of hydrolysis, hydrolysis of the above starting materials using the enzyme combination(s) under the aforementioned conditions and for the above period of time will generally result in a hydrolysate having the desired properties for use in the infant formula of the invention. Optionally, if necessary, the skilled person will be able - on the basis of the disclosure herein - to adapt the above hydrolysis conditions such that a hydrolysate with the desired properties is obtained.

[0077] Also, it should be noted that generally - and apart from the use of the above starting materials and preferred enzyme combination(s) - the hydrolysis conditions may not be too critical, dependant upon the manner in which the hydrolysate is (further) processed prior to use in the infant formula of the invention. However, it has been found that the desired characteristics a) to e) of the final infant formula are best and most reliably obtained when the above conditions are used in combination with the cooling step that will now be described.

[0078] The hydrolysis reaction may be terminated in any suitable manner. However, in order to ensure the combination of desired characteristics a) to e) in the final hydrolysate, it is most preferred that the hydrolysis reaction is not terminated/quenched by heating (as is usual), but instead by cooling the hydrolysis mixture, e.g. without specifically removing/denaturating the enzymatic activities present in the mixture.

[0079] In particular, according to the invention, the total reaction mixture is cooled within one hour from the hydrolysis temperature - e.g. about 45-60 °C, preferably between 50 and 58 °C - to a temperature of less than 20 °C, preferably less than 10 °C. Said cooling is preferably started between 1.5 to 3 hours after initiation of the hydrolysis reaction.

[0080] Thus, a suitable temperature protocol for the hydrolysis may be as follows:

- hydrolysis (45-60 °C, pref. 50-58 °C): 1.5 to 4 hours
- cooling (to <20 °C, pref. <10 °C): 10 min. to 1 hour
- total time: 1.7 to 4.5 hours

with the preferred temperature protocol for the hydrolysis being as follows:

- hydrolysis (45-60 °C, pref. 50-58 °C): 2.0 to 3.0 hours
- cooling (to <20 °C, pref. <10 °C): 10 minutes to 1 hour
- total time: 2.2 to 3.5 hours

[0081] The cooled hydrolysate thus obtained may then be used as such in the preparation of the infant formula of the invention, or after suitable processing, such as removing one or more undesired compounds or components, including but not limited to salts, amino acids, the enyzmes used in the hydrolysis.

[0082] This may for instance be carried out by desalting (e.g. by dialysis); by precipitation, i.e. through acidification with a food grade acid such as hydrochloric acid to a pH < 5,0, followed by removing of the precipitate (e.g. by centrifugation) and re-adjusting the pH to a suitable value, for example between 6 and 7; or by any other suitable technique.

[0083] Also, instead of the entire hydrolysate, only a fraction thereof may be used, for instance obtained by removing (part of) the proteins with a chain length of more than 30 amino acids.

[0084] The hydrolysate thus obtained is then incorporated into the infant formula of the invention, e.g. by the following non-limiting processing steps, which are preferably carried out within 24 hours, preferably within 8 hours, of the end of the hydrolysis reaction:

a) All further ingredients of the final formula - e.g. the lipid component(s) B; the prebiotic component(s) C (if any); eventually a part of the viscosity improver(s) D (if any); and the optional further components, such as the vitamins, minerals and trace elements - are added to the hydrolysate.
The mixture is then homogenised and heated, in order to obtain the desired microbiological quality of the product, without detracting (too much) from the desired characteristics of the formula and/or the desired biological activity of the components incorporated therein. For instance, a UHT treatment at 140 °C during about 2.4 seconds may be used. The product is then brought into a powder form - e.g. by evaporation and (spray-)drying. It is preferred that some of the ingredients such as the viscosity improving agents D - if present - are added to the powder after spraydrying. Then, the final composition can be aseptically packaged, e.g. in a suitable container such as a tin, a box, a bag, a flask or a sachet.
b) Alternatively, after adding the water-soluble components to be incorporated into the final formula - such as the vitamins, minerals and trace elements - the hydrolysate may be heated and partially dried/evaporated, upon which the lipid component(s) B and any remaining components are added. The mixture may then be homogenized and brought into powder form. After optionally adding further powdered ingredients such as viscosity increasing agents, the final composition is packaged, i.e. as described above.

[0085] An infant formula prepared in this manner - i.e. via the aforementioned method starting from the preferred hydrolysate - has optimum characteristics with respect to taste, low osmolality, low content of free amino acids, reduced sensibilizing characteristics, and a protein/amino acid content that is particularly suited for infant formula.

[0086] Also, in the method described above, the hydrolysate is subjected to only a minimal heat treatment, which

ensures that the biological activity of the components present in the formula is maintained, or at least not significantly detracted.

[0087] Furthermore, the above method reliably leads to a hydrolysate and/or infant formula with the desired characteristics, which is safe and is cost-efficiently produced (limited use of expensive enzymes such as Trypsin and low production costs).

[0088] Thus, in further aspects, the invention relates to a hydrolysate obtained via the method described in this Section II; to an infant formula comprising such a protein hydrolysate; and to the use of such a protein hydrolysate in the preparation of an infant formula, in particular to the use as component A in the preparation of an infant formula of the invention.

[0089] As above, the preferred hydrolysate is preferably present in the infant formula of the invention in an amount between 1 and 3 g/100 ml, more preferably between 1.3 and 2.0 g/100 ml, and most preferably between 1.6 and 1.9 g/ 100 ml of the total formula.

[0090] However, besides their use in the invention, it is envisaged that the method described in this Section II - as well as the hydrolysates obtained via said method - may find other applications, in particular in the field of food products, more in particular in the fields of infant foods and/or dietary foods, e.g. for the prevention or treatment of food allergies, and the manufacture of foods that are intended to rapidly pass the stomach and are easily digested. The latter products can be very useful for patients suffering from an impaired stomach function, an impaired liver function, an impaired panceas function and\or an impaired gut function.

[0091] Thus, as already mentioned, the method of this Section II as well as the hydrolysates obtained by it, form independant and separate aspects of the present invention.

III: Component B:

[0092] The at least one lipid component B - i.e. the one or more fats and/or fatty acid component(s) present in the infant formula of the invention - may be chosen from all fatty acid triglycerides known per se for use in food products, and are preferably chosen from all the fatty acid triglycerides and/or phospholipids (and/or mixtures thereof) known per se for use in infant foods, and in particular from those known per se for use in infant formulas.

[0093] As is known from the art, such fatty acid triglycerides generally comprise a glyceride molecule to which are attached, via ester bonds, three fatty acid residues, which may be the same or different, and which are generally chosen from saturated and unsaturated fatty acids containing 6 to 26 carbon atoms, including but not limited to linoleic acid, α-linolenic acid, oleic acid, palmitic acid (C_{16}) and/or stearic acid (C_{18}).

[0094] Such fatty acid triglycerides may differ in the fatty acid residues that are present and/or in the respective position(s) of the fatty acid residues (e.g. in the 1-, 2- and/or 3-position). Usually, as is known in the art, a lipid component for use in infant formula will comprise a suitable mixture of two or more, and usually a several, different fatty acid triglycerides, depending upon for instance the desired properties of the lipid component, the source of the fat, as well as the way in which the fat was obtained.

[0095] The at least one lipid component B - i.e. the one or more fatty acid triglycerides present therein - are preferably chosen such that the lipid component B is easily digestible by the infant, thereby (also) making the final formula easily digestible. This improves the structure of the faeces and improves the biological availablity of divalent cations such as calcium and/or the fats/fatty acids present in the formula.

[0096] In this respect, the amount and position of the palmitic acid residues that are present in the triglycerides that are present in/make up the at least one lipid component B are of special significance. Preferably, palmitic acid residues should make up more than 10 %, preferably 16 - 24 %, of all fatty acid residues present in the triglycerides used as or in component B.

[0097] Also, the amount of triglycerides in which the C_{14}:0, C_{16}:0 and/or C_{18}:0 fatty acids are in the Sn1 - or Sn3-position and in particular in which the palmitate residues are in the Snl or Sn3-position should be as low as possible. The amount of palmitic acid in the Sn1 or Sn3-position should preferably make up no more than 16 %, more preferably no more than 13 %, and most preferably no more 10.7 %, of all triglycerides present. This corresponds to amounts of triglycerides with the palmitate residue in the Sn1- or Sn3-position of less than 0.55 g/100 ml, preferably less than 0.50 g/100 ml, most preferably less than 0.38 g/100 ml of the infant formula of the invention.

[0098] In other - but somewhat less restrictive - words, when the palmitic acid residues make up more than 10%, preferably 16 - 24 % of all fatty acid residues present in the triglycerides used in or as component B of the invention, of these palmitic acid residues, as much as possible, and preferably at least 30%, more preferably at least 40 %, should be in the 2- or β-position of the triglyceride.

[0099] Mixtures of fatty acid triglycerides that contain more than 10 %, preferably 16 - 24 % palmitate residues and that meet one or both of the requirements relating to the position of the palmitate residues set out in the above two paragraphs, will also be referred to hereinbelow as the *"preferred lipid component B"*. For instance, these include specific phospholipids as well as so-called structured fats, e.g. fats of of animal or plant origin, in which the triglycerides

been subjected to enzymatic or other re-esterification such that the palmitic acid residues are for a large part present in the 2-position.

[0100] Such preferred components B are commercially available - e.g. from Loders Croklan under the name Betapol® - and/or can be prepared in a manner known per se., for instance as described in EP 0 698 078 and/or EP 0 758 846.

[0101] However, because of the better absorption of these fat mixtures from the infant gut, the use of a preferred lipid component B as described above may allow the amount of component B that is added to the infant formula of the invention to be reduced, while still providing sufficient energy/nutritional value to the infant.

[0102] In particular, by using a preferred lipid component B, the overall fat content of the infant formula of the invention may be reduced from 48 wt.% or more for conventional infant formulas to less than 46 wt.% in an infant formula of the invention.

[0103] Also, the use of a preferred lipid component B may allow the overall calcium content of the infant formula of the invention to be lowered, i.e. as set out above. Such a reduction in the calcium content may in turn allow the overall phosphorous-content of the infant formula of the invention to be lowered, again as set out above.

[0104] Alternatively, the use of a preferred lipid component B may allow the calcium-to-phosphorous ratio of the infant formula of the invention to be lowered, e.g. from about 2 for conventional formulas to a range of about 2.0 to 1.4.

[0105] Finally, although component B has been described above as essentially only consisting of fatty acid triglycerides, it should be understood that the presence of minor amounts of mono- or diglycerides (e.g. to a total of at most one-third of all fatty acids of all fatty acid mono-, di- and triglycerides present in or as component B, the remainder being fatty acid triglycerides to a total of 100% of component B) is not excluded. Such mono- or diglycerides will usually contain the fatty acid residues referred to above.

IV: Component C:

[0106] The one or more prebiotic components C may be chosen from all prebiotic components known per se for use in food products, and are preferably chosen from the prebiotic components known per se for use in infant foods, and in particular from those known per se for use in infant formulas.

[0107] Some preferred but non-limiting examples thereof include prebiotic oligosaccharides. Generally, these will be hydrolysed or non-hydrolysed carbohydrates comprising sugar residues interconnected via *beta* 1-1, 1-2, 1-3, 1-4, 1-6 and/or *alfa* 1-6 linkages. Most preferably, such oligosaccharides will contain 2-20 sugar residues in the saccharide backbone.

[0108] For instance, such prebiotic oligosaccharides include, but are not limited to, lacto-N-tetraose, lacto-N-fucopentaose, lactulose, lactosucrose, raffinose, galacto-oligosaccharides, fructo-oligosaccharides, oligosaccharides derived from soybean polysaccharides, mannose-based oligosaccharides, arabino-oligosaccharides, xylo-oligosaccharides, isomalto-oligosaccharides, glucans, sialyl oligosaccharides, fuco-oligosaccharides, and/or any suitable combination thereof.

[0109] Also, lactose may be used as the prebiotic. However, the use of lactose in the infant formula of the invention should be avoided when a formula with low lactose content is desired, e.g. a formula for infants that are, or are suspected to be, lactose intolerant (e.g. based on age or hereditary factors).

[0110] The use of one or more *trans*-galacto-oligosaccharides *("TOS')*, one or more fructo-oligosaccharides (*"FOS"*) and/or mixtures thereof is particularly preferred, in particular the use of mixtures of one or more trans-galacto-oligosaccharides and one or more fructo-oligosaccharides in which the ratio of TOS-to-FOS is between 5:1 and 15:1, and more in particular about 9:1, which mixtures generally provide a prebiotic effect comparable to mothers milk.

[0111] The amount(s) of the one or more prebiotic components C used will generally be dependant upon the specific prebiotic component(s) used, as well as on the amount for formula to be fed to the infant per day., e.g. as one or more, and preferably 4 *len*] or more, feedings per day.

[0112] Generally, the amount of prebiotic component(s) C will be such that - when the formula is fed to the infant in the amount recommended/prescribed - it is sufficient to provide a daily dose of prebiotic component(s) of at least 1.8 g/day for infants of less than 4 months old; and preferably at least 3.6 g/day for infants of more than 4 months old.

[0113] Normally, an infant will be fed a total of between 500- 800 ml of the formula of the invention per day. Thus, the above amounts correspond to an amount of component(s) C at least 0.3 g/100 ml of the total formula, more preferably at least 0.6 g/100 ml of the total formula.

[0114] The use of the above prebiotica in the infant formula of the invention may (help to) restore the natural gastrointestinal flora and/or will result in a reduction of aggresive components in the faeces, e.g. of components that may irritate or harm epithelial cells (such as those of the lining of the gastrointestinal tract and/or the skin). The latter is of extreme importance for infants suffering from diaper rash.

V: Component D:

[0115] The one or more viscosity improving components D may be chosen from all viscosity improving components known per se for use in food products, and are preferably chosen from the viscosity improving components known per se for use in infant foods, and in particular from those known per se for use in for infant formulas; see for example EP 0 846 422..

[0116] Some preferred but non-limiting examples thereof include viscosity improving components based upon carbohydrates, and in particular those based upon starches and/or starch derivatives such as pregelatinized starches, such as pregelatinized potato starch, which is preferred.

[0117] The amount(s) of the one or more viscosity improving component(s) D used will generally depend upon the specific viscosity improving component(s) used and on the other components present in the formula, and will generally be such that the viscosity of the final formula is between 20 and 100 cps, preferably between 40 and 80 cps; as measured in a Brookfield viscosimeter at 30 rpm. Usually, the total amount of viscosity improving component(s) D will be between 0.5 and 5 g/100 ml of the formula, preferably between 1 and 3 g/100 ml. For instance, pregelatinized potato starch may be used in an amount of between 1.4 and 2.1 g/100ml.

[0118] The use of the viscosity improving component(s) D may provide several advantages, including but not limited to prevention or reduction of regurgitation and/or excessive aerophagia (burps).

VI: Further components:

[0119] Besides the abovementioned components A to D, the invention may further contain any component or ingredient for infant formula known per se, in usual amounts (e.g. as prescribed by national or international guidelines) and depending upon (the properties of) the final formula desired. Such further components may include, but are not limited to, one or any combination of the following:

- one or more of the following compounds: taurine, choline, carnitine, inositol, biotine;
- one or more polyunsaturated long chain fatty acids ("PUFAs"), including but not limited to linoleic acid, α-linolenic acid, oleic acid, arachidonic acid and docosahexaenoic acid.
- one or more nucleotides and/or nucleotide analoga;
- one or more (added) amino acids, including but not limited to tryptophan and/or methionine.
- one or more (added) vitamins, including but not limited to vitamin K, vitamin B1, vitamin B2, vitamin A, vitamin E, vitamin D, vitamin C, niacine, pantothenic acid. Also, besides the usual amounts of these or other vitamins, the infant formula of the invention may also contain additional amounts of - for instance - folic acid, vitamin B 12 and/or vitamin B6;
- one or more minerals and/or trace elements;
- one or more preservatives (not preferred);
- one or more flavours and/or colorings.

Examples:

[0120] The invention will now be illustrated by means of the following non-limiting Examples 1-4, which described some infant formulas of the invention.

Example 1: Formula for infants of more than 4 months old.

[0121] An infant formula for infants of more than 4 months old is prepared essentially as described under II. above. The formula has the following composition, an energy/nutritional value of 72 kcal/ml and an osmolality of 260 mOsmol/l. The calcium content is 86 mg/100 kcal and the phosphorous content is 54 mg/100kcal.

Component	per 100 g powder	per 100 ml*
Protein equivalents	12.4	1.9 g
Whey-protein hydrolysate**		1.9
Carbohydrates	54.8	8.6 g

Notes: *: obtained by dissolving 15.6 g powder in 100 ml water.

**: preferred protein hydrolysate A as described under II. above.

(continued)

Component	per 100 g powder	per 100 ml*
Saccharides (lactose)		4.0 (2.7)
Polysaccharides from maltodextrines		2.0
Polysaccharides from potato starch		2.3
Organic acids		0.1
Fat	21.1	3.3 g (= 41 wt.%)
Saturated		1.4
Betapol (Unilever)		0.23
Mono-unsaturated		1.4
Poly-unsaturated		0.54
Fibre	5.0	0.78 g
TOS		0.7
FOS		0.08
Further components:		
Minerals, trace elements and vitamins by the EEC regulation 321.	in amounts as recommended	

Notes: *: obtained by dissolving 15.6 g powder in 100 ml water.

Example 2: Formula for infants of up to 6 months old.

[0122] An infant formula for infants of up to 6 months old is prepared essentially as described under II. above. The formula has the following composition, an energy/nutritional value of 70 kcal/ml and an osmolality of 240 mOsmol/l. The calcium content is 53 mg/100 kcal and the phosphorous content is 27 mg/100kcal.

Component	per 100 g powder	per 100 ml*
Protein equivalents	11.6	1.7 g
Whey-protein hydrolysate**		1.7
Carbohydrates	55.4	8.3 g
Saccharides (lactose)		4.0 (2.9)
Polysaccharides from maltodextrines		1.5
Polysaccharides from potato starch		1.8
Fat	21.1	3.3 g (= 42 wt.%)
Saturated		1.4
Betapol (Unilever)		0.23
Mono-unsaturated		1.4
Poly-unsaturated		0.54
Fibre	5.0	0.78 g
TOS		0.7
FOS		0.08
Further components:		
Minerals, trace elements and vitamins	in amounts as recommended by the EEC regulation 321.	

Notes: *: obtained by dissolving 15.0 g powder in 100 ml water.
**: preferred protein hydrolysate A as described under II. above.

Example 3: Formula for infants of up to 4 months old.

[0123] An infant formula for infants of up to 4 months old is prepared essentially as described under II. above. The formula has the following composition, an energy/nutritional value of 67 kcal/ml and an osmolality of 230 mOsmol/l. The calcium content is 45 mg/100 kcal and the phosphorous content is 25 mg/100kcal.

Component	per 100 g powder	per 100 ml*
Protein equivalents	10.5	1.54 g
Hydrolysed whey**		1.46
From L-tryptophan		0.01
From L-methionine		0.01
From hydrolysed baker's yeast**		0.06
Carbohydrates	55.4	8.3 g
Saccharides (lactose)		3.5
Polysaccharides from maltodextrines		3.3
Polysaccharides from potato starch		1.4
Fat	19.2	3.0 g (= 40 wt.%)
Saturated		1.2
Betapol (Unilever)		0.23
Mono-unsaturated		1.3
Poly-unsaturated		0.5
Fibre	3.2	0.5 g
TOS		0.37
FOS		0.03
Lacto-N-tetraose		0.10
Further components:		
Folic acid (µg)		20
Vitamin K (µg)		10
Minerals, trace elements and vitamins	in amounts as recommended by the EEC regulation 321.	

Notes: *: obtained by dissolving 15.0 g powder in 100 ml water.
**: preferred protein hydrolysate A as described under II. above.

Example 4: Formula for infants of up to 4 months old.

[0124] An infant formula for infants of up to 4 months old is prepared essentially as described under II. above. The formula has the following composition, an energy/nutritional value of 68 kcal/100 ml and an osmolality of 260 mOsmol/l. The calcium content is 40 mg/100 kcal and the phosphorous content is 20 mg/100kcal.

Component	per 100 ml*
Protein equivalents	1.30 g
Hydrolysed β-casein/whey (40/60)	1.29
From L-tryptophan	0.01
Carbohydrates	8.5 g
Lactose	5.5
Polysaccharides	2.8

Notes: *: obtained by dissolving 14.5 g powder in 100 ml water.
**: preferred protein hydrolysate A as described under II. above.

(continued)

Component	per 100 ml*
Lipids	3.2 g
Saturated	1.5
From β-palmitate	0.2
From MCT's + coconut oil	1.1
Mono-unsaturated	1.2
Poly-unsaturated	0.5
Fibre	0.5 g
Arabino oligosaccharides	0.4
FOS	0.1
Further components:	
Minerals, trace elements and vitamins	in amounts as recommended by the EEC regulation 321.

Notes: *: obtained by dissolving 14.5 g powder in 100 ml water.
**: preferred protein hydrolysate A as described under II. above.

Claims

1. Infant formula, comprising

a) at least one protein component; and
b) at least one lipid component that can be easily digested by an infant;

and optionally one or two of:

c) at least one prebiotic component;
d) at least one viscosity improving component;

and optionally one or more components of infant formula known per se,
characterised in that:
the protein component a) has a phosphorous content of less than 0.75 g P/100 g protein, preferably less than 0.72 g P/100 g protein, and even more preferably less than 0.69 g P/100 g protein.

2. Infant formula according to claim 1, further characterised in that:
the at least one lipid component b) comprises at least one fatty acid triglyceride and/or a mixture of fatty acid triglycerides, in which:

- palmitic acid residues make up more than 10 %, preferably 16 - 24 % of all fatty acid residues present in the triglycerides; and in which:
- the triglycerides in which the palmitate residue is in the Sn1- or Sn3-position make up no more than 16 %, preferably no more than 13 %, more preferably no more than 10.7 %, of all triglycerides present.

3. Infant formula according to claim 1 and/or 2, in which the at least one protein component a) has been derived from mammalian milk.

4. Infant formula according to any of claims 1-3, in which the at least one protein component a) is a hydrolysate obtained by hydrolysing a starting material comprising proteins from mammalian milk or a dephosphorylated protein from plant origin with a combination of at least one endo- and at least one exoproteinase.

5. Infant formula according to claim 4, in which hydrolysate used as component a) is obtained by hydrolysing a starting material comprising a milk protein, a mixture of milk proteins and/or a milk protein preparation with a

combination of at least one endo- and at least one exoproteinase;

6. Infant formula, in particular according to one of claims 1-5, comprising:

e) at least one protein component; and
f) at least one lipid component that can be easily digested by an infant;

and optionally one or two of:

g) at least one prebiotic component;
h) at least one viscosity improving component;

and optionally one or more components of infant formula known per se,
characterised in that:
the at least one protein component a) is a protein hydrolysate, obtained by hydrolysing a starting material comprising a milk protein, a mixture of milk proteins and/or a milk protein preparation with a combination of at least one endo- and at least one exoproteinase;
and further characterised in that:
the at least one lipid component b) comprises at least one fatty acid triglyceride and/or a mixture of fatty acid triglycerides, in which:

- palmitic acid residues make up more than 10 %, preferably 16 - 24 % of all fatty acid residues present in the triglycerides; and in which:
- the triglycerides in which the palmitate residue is in the Sn1- or Sn3-position make up no more than 16 %, preferably no more than 13 %, more preferably no more than 10.7 %, of all triglycerides present.

7. Infant formula according to claim 6, comprising:

a) the at least one protein hydrolysate;
b) at least one lipid component that can be easily digested by an infant;
c) at least one prebiotic component;
d) at least one viscosity improving component;

and optionally one or more components of infant formula known per se.

8. Infant formula according to any of the preceding claims, characterised by a content of free amino acids, derived from the protein hydrolysate a), of less than 10 g, and preferably less than 7 g per 100 g protein equivalent.

9. Infant formula according to any of the preceding claims, characterised by an osmolality of less than 270 mOsmol/l, preferably less than 240 mOsmol/l, most preferably less than 230 mOsmol/l;

10. Infant formula according to any of the preceding claims, intended for infants of less than 6 months old, characterised by a calcium content (expressed as mg of calcium per 100 kcal of energy content of the formula) of less than 80 mg/100kcal, and preferably less than 77 mg/100 kcal.

11. Infant formula according to any of the preceding claims, intended for infants of more less than 6 months old, characterised by a calcium content (expressed as mg of calcium per 100 kcal of energy content of the formula) of less than 122 mg/100kcal, and preferably less than 116 mg/100 kcal.

12. Infant formula according to any of claims 1-4, characterised by a calcium-to-phosphorous ratio of between 1.4 and 2.

13. Infant formula according to any of the preceding claims, characterised by an overall fat content (expressed as total lipid content) of less than 45 wt.%.

14. Infant formula according to any of the preceding claims, characterised in that the relative amounts of the components a) to d) and the one or more further components are:

- the at least one protein component a): 6.4 to 16 wt.%
- the at least one lipid component b): 18 to 29 wt.%
- at least one prebiotic component c): 0 to 15 wt.%
- at least one viscosity improving component d): 0 to 15 wt.%
- one or more further components: 0 to 60 wt.%

to a total of 100 wt.% of the final formula.

14. Infant formula according to any of the preceding claims, characterised in that the relative amounts of the components a) to d) and the one or more further components are:

- the at least one protein componen a): 6.4 to 16 wt.%
- the at least one lipid component b): 18 to 29 wt.%
- at least one prebiotic component c): 3.0 to 15 wt.%
- at least one viscosity improving component d): 1.5 to 15 wt.%
- one or more further components: 0 to 60 wt.%

to a total of 100 wt.% of the final formula.

16. Infant formula according to any of the preceding claims, characterised by a viscosity of between 20 and 100 cps, more preferably between 40 and 80 cps; as measured in a Brookfield viscosimeter at 30 rpm.

17. Infant formula according to any of the preceding claims, characterised by a lactose content of at most 6,0 g/100 ml, preferably at most 4,5 g/100ml, most preferably less than 3,0 g/100 ml of the total formula, as determined by an assay for lactose content known per se.

18. Method for preparing a protein hydrolysate, comprising hydrolysing a protein starting material that has a phosphorous content of less than 0.75 g P/100 g protein, preferably less than 0.72 g P/100 g protein, and even more preferably less than 0.69 g P/100 g protein, with a combination of at least one endo- and at least one exoproteinase.

19. Method for preparing a protein hydrolysate, in particular according to claim 18, comprising hydrolysing a starting material comprising a milk protein, a mixture of milk proteins, and/or a milk protein preparation with a combination of at least one endo- and at least one exoproteinase,

20. Method according to claim 18 or 19, in which said enzyme mixture is added in an amount of 0.1-5 %, based on the starting material.

21. Method according to any of claims 18-20, in which proteins from mammal milk, in particular from bovine milk, such as whey, in particular acid whey; dephosphorylized casein; or a suitable mixture thereof is used as the starting material.

22. Method according to any of claims 18-21, in which the starting material further contains a suspension of yeast cells, optionally homogenized and heated and/or pre-treated to crush the cell walls, in an amount of 1 to 8 g dry mass of yeast cells per 100 g protein.

23. Method according to any of claims 18-22, in which the mixture of the at least one endo- and at least one exoproteinase is a mixture containing the enzymes Alcalase®, Trypsine® and Flavourzyme® is used.

24. Method according to claim 23, in which the enzymes Alcalase, Flavourzyme and Trypsine are used in a relative amounts of about 5-10 parts Alcalase to 3-5 parts Flavourzyme to 1 part Trypsine, and in which said mixture is used in an amount corresponding to at least 0.1% Trypsine per 100 g of starting material.

25. Method according to claim 23 or 24, in which the hydrolysis is carried out as follows:

- pH: kept essentially constant in the range of 6.4 to 8, preferably 6.8 to 7.8;
- temperature of hydrolysis: between 45 and 60 °C, preferably between 50 and 58 °C.
- time of hydrolysis: 1.5 to 4 hours.

26. Method according to any of claims 18-25, and in particular according to one of claims 23-25, in which the hydrolysis reaction in terminated by cooling the total hydrolysis mixture from the hydrolysis temperature to a temperature of less than 20 °C, preferably less than 10 °C, over a period of time of 10 min. to 1 hour.

27. Method according to any of claims 18-26, further comprising at least one step of processing the mixture obtained from the hydrolysis reaction, such as removing one or more undesired compounds or components.

28. Hydrolysate, obtained via the method of any of claims 18-27.

29. Infant formula, comprising a protein hydrolysate of claim 28.

30. Infant formula according to claim 29, further comprising

b) at least one lipid component that can be easily digested by an infant; and optionally one or two of:
c) at least one prebiotic component;
d) at least one viscosity improving component;

and optionally one or more components of infant formula known per se,

31. Use of a protein hydrolysate of claim 28 in the preparation of an infant formula, in particular in the preparation of an infant formula of one of claims 1-17.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 99 20 4287

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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	10 May 2000	Rooney, K

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